Remarks

Rejection Under 35 U.S.C. § 112, first paragraph, enablement

Claims 1-3, 19, 29-31 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended. Claim 2 is canceled, and therefore the rejection of claim 2 is moot.

Claim 1 is amended to clarify that the agent is selected from the group consisting of a β receptor blocker or a compound which inhibits the effect of aldosterone. Basis for the amendment is found in the specification as originally filed, for example the paragraph bridging pages 2 and 3. Claim 3 is amended to depend from claim 1. Claims 19 and 29-31 also depend from claim 1.

The Examiner acknowledges that the method of treating the symptoms of cachexia by administering a beta blocker or compounds that inhibit the effects of aldosterone is enabled. Thus, claims, 1, 3, 19 and 29-31 as amended are enabled and the rejection should be withdrawn.

Rejection Under 35 U.S.C. § 112, first paragraph, written description

Claims 1-4 and 19 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Examiner concluded that the genus of claim 1 was not supported in the specification with a sufficient number of species. This rejection is traversed, but to facilitate prosecution and without making any admission, Claim 1 as amended identifies the agent as a beta receptor blocker or a compound that inhibits the effects of aldosterone. The Examiner acknowledges that the specification establishes a correlation between both beta blockers and aldosterone antagonists and cachexia. Therefore claim 1 as amended meets the written description requirement, and the rejection should be withdrawn.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-4, 19, and 29-31 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended. Claim 2 is canceled; therefore, the rejection of claim 2 is moot.

Independent claim 1 as amended requires that the agent is selected from a beta receptor blocker or a compound that inhibits the effect of aldosterone. The Examiner rejected the previous claims because the term "sympathetic nervous [system] activity" is indefinite . The specification allegedly does not describe which sympathetic nervous system activity is being referred to.

One of Skill in the Art Would Understand the Meaning and Scope of the Term "Sympathetic Nervous System Activity"

One of ordinary skill in the art would understand the meaning of the term "sympathetic nervous system activity" based on the knowledge available at the time the application was filed in combination with the guidance provided in the specification as originally filed. As noted in the previously submitted 37 C.F.R. § 1.132 declarations, one of ordinary skill in the art would be

a physician or Ph.D. practicing in the field. Such a person would be familiar with textbooks such as Anatomy & Physiology, (Seeley, Rod. R., et al., 4th ed.) p. 511, WBC/McGraw Hill: New York, 1998). Page 511, Table 16.3 of this textbook discloses sympathetic nervous system activity (copy enclosed). Stimulating the sympathetic nervous system results in constriction of blood vessels and the release of catecholamines such as epinephrine and norepinephrine, among other activities. Thus, one of ordinary skill in the art would understand the meaning and scope of the term "sympathetic nervous system activity", and the rejection should be withdrawn.

The Specification Identifies Specific Sympathetic Nervous System Activities

The specification explicitly discloses that beta receptor blockers are agents that reduce catecholamine levels (p. 5, lines 8-11). Catecholamines include adrenalin (epinephrine), noradenalin (norepinephrin), and dopamine (a precursor molecule for norepinephrine) (p. 22, line 13). The specification also discloses that the measurement of catecholamine levels is the preferred method for measuring sympathetic nervous system activity (p. 22, line 11 to page 23, line 12).

With regard to compounds that inhibit the effect of aldosterone, the specification discloses that aldosterone antagonists may prevent or reduce myocardial and skeletal muscle fibrosis which enables muscle to act more efficiently and thereby prevent or reduce the stimulus for sympathetic nervous system reflex abnormalities (p. 14, lines 13-17). Thus, the specification identifies a sympathetic nervous system activity that is mediated by the claimed agents. In view of the foregoing remarks, the rejection should be withdrawn.

Rejection Under 35 U.S.C. § 102

Claims 1-4, 19, and 29-31 were rejected under 35 U.S.C. § 102(b) as being anticipated by RALES investigators, "Effectiveness of *Spironolactone* added to an angiostensin-converting enzyme inhibitor and a loop diuretic for severe chronic congestive heart failure (The Randomized Aldactone Evaluation Study [RALES]" *The American Journal of Cardiology* 78:902-907 (1996)("RALES"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

As discussed above, independent claim 1 is amended to identify the agents as a beta receptor blocker or a compound that inhibits the effects of aldosterone. Claim 4 identifies spironolactone as an aldosterone inhibitor.

The Examiner rejected the claims as anticipated by RALES because RALES discloses a method of administering spironolactone to patients with severe congestive heart failure who had symptoms of congestive heart failure classes II-IV of New York Heart Association Functional Classification. The Examiner reasoned that some of the patients ***might be*** cachectic given their classification. Moreover, the Examiner argues that there is ***no way to rule out*** that some of the patients that had NYHA class II-IV were not cachectic. Whether an element of the claims might be present in a reference or whether there is no way to exclude that an element might not be in a reference is not the proper standard for rejection claims under 35 U.S.C. § 102(b).

RALES Fails to Expressly Disclose Each Element of the Claims

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v.*

Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The Examiner acknowledges that the RALES study did not select cachectic patients per se. Thus, the Examiner concedes that RALES does not expressly disclose each and every element of the claims because RALES fails to disclose a method for treating cachecia. In fact, RALES discloses that some patients actually lost weight when treated with spironolactone. On page 904, RALES provides:

> At the day 9 and week 4 visits, there were statistically significant dose responses with respect to changes from baseline in body weight: patients in the 75-mg dose group of spironolactone therapy **lost more weight than did other patients**. This dose response was not observed at later visits ($p \geq 0.06$). (emphasis added).

Thus, contrary to the Examiner's position, RALES not only fails to disclose treating cachexia, RALES discloses that treatment with 75 mg/d actually causes patients with chronic heart failure (but who do not necessarily have cachexia, as discussed further below) to lose weight.

RALES Fails to Inherently Disclose Each Element of the Claims

The Examiner argues that although RALES does not expressly disclose treating cachexia, there is no way to rule out that some of the patients treated in RALES had cachexia. The Examiner appears to suggest that RALES inherently discloses treating cachexia because some of the patients were NYHA class II-IV. It is important to note that as provided in the previous response, not all patients with heart failure have cachexia (see page 27, lines 15-16; see also Hunt, et al., "ACC/AHA guidelines for the evaluation and management of chronic heart failure

in the adult: executive summary" *Journal of the American College of Cardiology* 38:7 (2102-2113 (2001) page 2109, first column).

The Court of Appeals for the Federal Circuit has made clear that the fact that a certain result or characteristic ***may*** occur or be present in the prior art ***is not sufficient to establish the inherency of that result or characteristic.*** *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). See MPEP § 2112.

The Examiner's rationale for rejecting the claims is based, at least in part, on the reasoning that some of the patients in the RALES study ***might*** be cachectic. This conclusion is clearly against the holdings of the Federal Circuit as discussed above. Moreover, the Examiner has failed to show that the patients in the RALES study ***necessarily*** were cachectic. The mere fact that some of the patients were NYHA class II-IV does not necessarily mean that the patients were cachectic. Indeed the NYHA classification does not even mention weight loss or cachexia.

The NYHA functional classification classifies the extent of heart failure, and places patients in one of four of the following categories:

I. No symptoms and no limitation in ordinary physical activity.
II. Mild symptoms and slight limitation during ordinary activity.
Comfortable at rest.
III. Marked limitation in activity due to symptoms, even during less-than-ordinary activity.
Comfortable only at rest.
IV. Severe limitations. Experiences symptoms even while at rest.

(See enclosed print out from Wikipedia). Thus, whether a patient has cachexia or not is irrelevant to their NYHA classification.

Because the patients in RALES do not necessarily have cachexia, RALES does not inherently disclose a method for treating cachexia, and the rejection should be withdrawn.

Objections to the Specification

The Examiner objected to the specification because the deletion of Examples 6-9 allegedly introduces new matter by omission. Applicants have filed a Petition to the Director to review the Examiner's conclusion that the amendments to the specification introduced new matter by omission.

The Examiner also objected to the drawings alleging that the amended drawings were not labeled "Replacement Sheets". A review of the drawings filed on April 14, 2006, on PAIR shows that the drawings were in fact labeled "Replacement Sheets". Accordingly, the objection should be withdrawn. To expedite prosecution, Applicants enclose a photocopy of the drawings submitted on April 14, 2006. The Examiner's attention is directed to the label on the top of the

sheet. The last sentence of the label reads "Replacement Sheet". Applicants respectfully request that the amendment to the drawings be entered.

Amendments to the Claims

Claims 2, 5-9, 11-18, 22-28, and 32-47 are canceled without prejudice or disclaimer.

Allowance of claims 1, 3, 4, 10, 19-21, and 29-31, as amended, is respectfully solicited.

Respectfully submitted,

/Patrea L. Pabst
Patrea L. Pabst
Reg. No. 31,284

Date: October 30, 2006

PABST PATENT GROUP LLP
400 Colony Square, Suite 1200
1201 Peachtree Street
Atlanta, Georgia 30361
(404) 879-2151
(404) 879-2160 (Facsimile)